ABSTRACTS

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Prevalence of and risk factors for peripheral arterial disease in the United States: Results from the National Health and Nutrition Examination Survey, 1999-2000

Selvin E, Erlinger TP. Circulation 2004;110:738-43.

Conclusion: Peripheral arterial disease (PAD) affects more than 5 million adults in the United States, increases dramatically with age, and disproportionately affects blacks. A large majority of patients with PAD have one or more cardiovascular risk factors.

Summary: Data from 2174 participants in the 1999-2000 National Health and Nutrition Examination Survey who were age 40 years or older were analyzed. PAD was determined to be present if the ankle brachial index was less than 0.9 in either leg. The prevalence of PAD in the population of adults aged over 40 in the United States was 4.3% (95% confidence interval [CI], 3.1% to 5.1%) corresponding to approximately 5 million individuals. Among subjects aged 70 years or older, the prevalence was 14.5% (95% CI, 10.8% to 18.2%). A gender- and age-adjusted logistic regression analysis indicated black race/ethnicity (odds ratio [OR], 2.83; 95% CI, 1.48 to 5.42), current smoking (OR, 4.46; 95% CI, 2.25 to 8.84), diabetes mellitus (OR, 2.72; 95% CI, 1.03 to 7.12), hypertension (OR, 1.75; 95% CI, 0.97 to 3.13), hypercholesterolemia (OR, 1.68; 95% CI, 1.09 to 2.57), and diminished kidney function (OR, 2.00; 95% CI, 1.08 to 3.70) were associated with PAD. One or more cardiovascular risk factors were present in 95% of persons with PAD. Elevated C-reactive protein levels and fibrinogen were also associated with PAD.

Comment: If anything, the study likely underestimates the prevalence of PAD, as patients with severe risk factors or severe chronic disease may have been less likely to participate in the survey.

Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysms (EVAR Trial I), thirty-day operative mortality results: Randomised controlled trial

EVAR Trial Participants. Lancet 2004;364:843-8.

Conclusion: In patients with large abdominal aortic aneurysms (AAA) anatomically suitable for either open or endovascular aneurysm repair (EVAR), EVAR reduces the 30-day operative mortality rate by two thirds compared with open repair.

Summary: This is a large, multicenter, prospective randomized study from 41 British hospitals comparing EVAR to open aneurysm repair. Between 1999 and 2003, 1082 elective (nonemergency) patients were randomized to receive either EVAR (n = 543) or open AAA repair (n = 539). All patients were at least 60 years of age with aneurysm diameters of 5.5 cm or more. All patients were required to be medically and anatomically suitable for either open AAA repair or EVAR. This is a preliminary report of this study in which the primary outcome measure is all-cause mortality. The analysis presented in this paper is operative mortality by intension to treat and a secondary analysis in patients actually treated per protocol.

The study enrolled 983 men and 99 women with a mean age of 74 years ± 6 years and a mean AAA diameter of 6.5 cm ± 1 cm. Of these patients, 1047 (97%) underwent AAA repair, and 93% (n = 1008) received their allocated treatment. In the EVAR group, 30-day mortality was 1.7% (9/521) versus 4.7% (24/516) in the open repair group (odds ratio [OR], 0.35; 95% confidence interval [CI], 0.16 to 0.77; $P = 0.009$). With a per protocol analysis, 30-day mortality for EVAR was 1.6% (8/512) versus 4.6% (23/496) for open repair (OR, 0.33; 95% CI, 0.15 to 0.74; $P = .007$). EVAR patients received more secondary interventions than open aneurysm repair patients (9.8% vs 5.8%, $P = .02$).

Comment: This trial and the Dutch Randomised Endovascular Aneurysm Management (DREAM) Trial (see below) (N Engl J Med 2004;351: 1607-18) deliver a clear message. Endovascular AAA repair has a lower risk for 30-day mortality than open aneurysm repair. The durability of EVAR remains in doubt, however, and there are data to suggest that the ongoing risk of rupture with EVAR, even though low, will rapidly lead to obliteration of the perioperative benefit of operative mortality. The need for secondary procedures in the EVAR patients and the costs of ongoing treatment and monitoring also remain significant questions. At this point the results of this trial and the Dream Trial do not mandate change in clinical practice.

A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms

Prinssen M, Verhoeven ELG, Buth J, et al. N Engl J Med 2004;351: 1607-18.

Conclusion: The authors conclude that endovascular repair is preferable to open repair in patients who have an abdominal aortic aneurysm (AAA) that is at least 5 cm in diameter. The authors' data do not substantiate this conclusion (see aComment@ below).

Summary: This was a multicenter randomized trial that compared endovascular repair and open repair of AAAs in 345 patients where the aneurysms measured at least 5 cm in diameter in patients who were candidates for either endovascular or open repair. End points included operative (30-day) mortality and two composite end points consisting of either operative mortality and severe complications or operative mortality and moderate or severe complications.

Eight of 174 patients undergoing open repair died within 30 days (operative mortality, 6.4%) of the procedure. Two of 171 patients undergoing endovascular repair died within 30 days (operative mortality, 1.2%) of the procedure (risk ratio [RR], 3.9; 95% confidence interval [CI], 0.9 to 32.9, $P = .10$). The combined rate of operative mortality and severe complications was 4.7% in the endovascular group versus 9.8% in the open repair group (RR, 2.1; 95% CI, 0.92 to 5.4; $P = .10$). The combined rate of operative mortality and moderate or severe complications was 23.6% in the open repair group versus 18.1% in the endovascular repair group (RR, 1.3; 95% CI, 0.9 to 2.0; $P = 0.23$.

Comment: This study and the larger Endovascular Aneurysm Repair (EVAR) trial (Lancet 2004;364:843-8) both document lowered 30-day mortality rates with endovascular aneurysm repair versus open AAA repair. However, it is not possible to truly compare endovascular repair and open repair without long-term data regarding the risk of aneurysm rupture, graft complications, need for follow-up, and cost. There are also indications that larger aneurysms repaired with endovascular techniques may not do as well in the long run as the smaller aneurysms (JVS 2003;137:1206-12). All of these concerns, in combination with the recent suppression of a US Food and Drug Administration Report under pressure from industry (JVS 2004; 40:209-10), combine to lead one to question the authors' conclusions in the abstract of this article. An insightful editorial on these arguments by Dr Frank Lederle is included in the same issue of the *New England Journal of Medicine* (N Engl J Med 2004;351:1677-9) and is recommended to readers of the *Journal of Vascular Surgery.*

Improved vascular gene transfer with a helper-dependent adenoviral vector

Wen S, Graf S, Massey P.G., et al. Circulation 2004;110:1484-91.

Conclusion: A third-generation or "helper-dependent" adenoviral vector can stably express a therapeutic gene in the vascular wall for more than 8 weeks.

Summary: Adenoviral vectors can be used to transfer genes into the vascular wall. The utility of adenoviral vectors for vascular gene transfer has been limited by host inflammatory response and limited periods of expression of the gene. In this study, a third-generation or helper-dependent adenoviral vector that has achieved prolonged recombinant gene expression in liver and muscle with minimal associated inflammation was tested for vascular gene transfer. A helper-dependent adenoviral vector expressing rabbit urokinase plasminogen activator (HD-AduPA) was studied. The third-generation helper-dependent adenoviral vector expressing HD-AduPA was compared with a first-generation adenovirus also expressing rabbit urokinase plasminogen activator (FG-AduPA). Urokinase plasminogen activator and vector-delivered DNA were measured in arteries harvested 3 to 56 days after gene transfer. Vector-specific mRNA, neointimal formation, and vascular inflammation were examined 14 days after gene transfer.

Urokinase plasminogen activator expression was lost and vector DNA declined rapidly in arteries treated with FG-AduPA. However, urokinase plasminogen activator expression and vector DNA persisted in HD-AduPA arteries for 56 days or more. Expression was stable from 14 to 56 days. Increased urokinase plasminogen activator in HD-AduPA arteries was also associated with high levels of vector-specific urokinase plasminogen activator and mRNA. There was less information in arteries treated with HD-AduPA than those treated with FG-AduPA. There was also less neointimal formation in the HD-AduPA–treated arteries.

Comment: The Holy Grail of gene therapy is to transfer a therapeutic gene to an individual requiring the gene product with subsequent stable expression of the gene product and minimal adverse reaction of the host. Research such as this is crucial to making gene therapy a therapeutic reality.